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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,491	02/10/2004	Alan H. Posner		1426

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EXAMINER	
UNDERDAHL, THANE E	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/775,491	POSNER ET AL.	
	Examiner	Art Unit	
	Thane Underdahl	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims contain the limitation of "specified limits" (claim 1) and "target concentration" (claim 6) for the concentration of hemoglobin in a solution. These terms are not defined in the specification and could be the physiological concentration of hemoglobin or highly concentrated solutions that will be used for diagnostic kits. Since protein concentrations have an effect on storage and reaction conditions, one of ordinary skill in the art requires a range of concentrations with these terms. (Reference X, Pierce, Protein stability and storage)

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1, 2, 4-7 and 9 are rejected under 35 U.S.C. 103(a) as being obvious over Bleile et al. (U.S. Patent # 4,448,888, Reference A) in combination with Fiechtner et al. (Reference B, U.S. Patent # 5,589,393).

3. These claims are drawn to preparation of a liquid stable glycosylated hemoglobin (Hemoglobin A1C or HbA1C). Claim 1 specifically mentions the steps comprising the isolation of the HbA1C, while claim 2 provides an additional step of adding a cyanide salt which will prevent microbial contamination (claim 4) and the formation of methemoglobin (claim 5).

4. Bleile et al. teach the isolation of high concentrations of Hemoglobin A1C from whole human blood. (Bleile et al. col 6, line 45) The red blood cells (RBC) are centrifuged and the plasma is removed. (step 1) The cells are washed 4 times with isotonic saline (0.15 M NaCl) and the supernatants were removed by aspiration. (step 2) The washed cells were pooled and lysed by adding sterile-filtered deionized water. (step 3). They complete the cell lysis by lowering the pH and stirring the mixture. Once the cells are lysed Bleile et al. continues to teach the 6^{th}, 7^{th}, 9^{th} and 10^{th} steps by centrifuging the lysis reaction mixture (step 6) and drawing off and filtering the hemolysate in a laminar flow hood (step 7) and dialyzing the hemolysate with a cellulose tubing (step 9).

5. In step 2 where the applicant claims to wash the RBC cells three times and the reference teaches four washings. One of ordinary skill in the art would recognize that the purpose of washing the cells is to remove soluble matter from the isolated cells. The skilled artisan would recognize that the volume of the liquid used to wash as well as the

number of repetitions are variable as long as the artist is reasonably assured that the soluble matter is removed. A person of ordinary skill in the art would recognize that these two variables are a matter or routine optimization on the part of the artisan. (M.P.E.P. § 2145.05 B)

Claims 2, 4, 5, 7 and 9 are taught by Bleile et al., who add potassium cyanide after the hemolysate is isolated. (claims 2 and 7) (col 6, line 69) The potassium cyanide also acts as a preservative against microbial contamination since cyanide and azide are known to inhibit cellular growth as supported by Morgan. (Reference U, Morgan page 27, col 1, 1st paragraph) (claims 4 and 9) The cyanide salt will reduce the formation of methemoglobin (metHb) as supported by Rodkey. (Reference V, Clinical Chemistry 22 (1976) 1986) (claim 5) Rodkey teach that the addition of potassium cyanide inhibits the formation of metHb in the presence of nitrite. (Rodkey, see abstract, table 2 and figure 4)

6. What Bleile et al. does not teach is the method steps 4, 5, 8, and 10, of claim 1 which freeze and then defrost the cells to produce the hemolysate, (steps 4 and 5) heat the hemolysate to degrade the labile HbA1C (step 8), and adjust the concentration of Hb in the hemolysate (step 10). Also, Bleile does not teach claim 6, which is the addition of glucose to the hemolysate and heating to produce glycosylated hemoglobin to a target concentration. These are taught by Fiechtner et al. (Reference B, U.S. Patent # 5,589,393).

7. Fiechtner et al. teach the freezing of the lysate solution (step 4) and then thawing the solution to complete the cell lysis (step 5). (Fiechtner et al., col 15, line 63)

Fiechtner et al. teach the heating of the hemolysate with and without glucose to produce liquid stable glycated hemoglobin. (col 16-18, Examples 3 and 4) These solutions were incubated at 37 °C prior to diafiltering. (Claim 1 step 8 and claim 6) (col 17, line 25 and line 44) When no glucose was added to the solution, the specified concentration of hemoglobin was adjusted to 19.5 g/dL. (col 17, line 18) When glucose was added the solutions were incubated until 7.5% to 97.2 % of the hemoglobin was glycated. (col 18, Table 3) The duration of time they heated the reaction at 37 °C was between 7 and 336 hours. (col 18, table 3) This is more than enough time to reduce the labile form of hemoglobin A1c as supported by Naka who suggests 4 hours. (Claim 1 step 8 and claim 6) (Reference C, U.S. Patent # 5,474,677, col 2, line 1)

8. Bleile et al. and Fiechtner et al., share the stated goals of producing a hemolysate for analysis of HbA1C and use the same starting materials (RBC) and use similar method steps such as washing the cells in isotonic solutions to achieve these goals. It would have been obvious to someone skilled in the art that since the two patented methods share and achieve the same goals using similar steps and materials that the two methods contain interchangeable steps. One of ordinary skill would be motivated to insert steps of Fiechtner et al., into the method of Bleile, or visa versa to create a more efficient process overall for obtaining hemolysate to analyze Hb1AC. The reasonable expectation of success is provided by both Fiechtner et al., and Bleile who successfully create hemolysate sufficient for their experiments.

In conclusion, for the reason given above, claims 1, 2, 4-7 and 9 are taught by the combination of the Bleile et al., and Fietchtner et al. who teach share methods for

the isolation or analysis of HbA1C. Therefore, the invention as a whole would have been prima facie obvious at the time of filing.

Claims 3 and 8 are rejected under 35 U.S.C. 103(a) as being obvious over Bleile et al., and Fietchtner et al. as applied to claims 1, 2, 4-7 and 9 and in further view of Mortenson (Reference W, J. of Chromatography, vol 182, page 325).

These claims are drawn to the addition of carbon monoxide to ensure the physical appearance of the product.

Bleile et al. and Fietchtner et al. together teach the isolation of HbA1C but do not teach the step of adding of carbon monoxide to the hemolysate. This is taught by Mortensen.

Mortensen teach that treating the hemolysate with carbon monoxide will ensure stability for 1 year. (Mortensen, page 326 "Preparation of the hemolysates") The paper by Mortenson, like Bleile et al. and Fietchtner et al., teach a method to quantitatively determine HbA1C in blood samples to determine the diabetic history of the patient. (Mortenson, page 325 abstract) Mortenson also uses several of the same process steps as Bleile and Fietchtner et al. in obtaining the hemolysate. It would therefore have been obvious for the person of ordinary skill in the art to add carbon monoxide to the hemolysate obtained to the procedures of Bleile and Fietchtner et al. to ensure the long-term stability of HbA1C. One would be motivated by Mortenson who teach that the hemolysate is stabile as a liquid for 1 year. One would have reasonable expectation of success base on Mortenson who produced a hemolysate with similar steps to Fietchtner et al. and Bliele that was sufficient to measure HbA1C in their experiments.

In summary no claims, as written, are allowed for this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thane Underdahl whose telephone number is (571) 272-9042. The examiner can normally be reached on 8:00 to 17:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Thane Underdahl
Art Unit 1651

SANDRA E. SAUCIER
PRIMARY EXAMINER